

Promotion of Human Early Embryonic Development and Blastocyst Outgrowth In Vitro Using Autocrine/Paracrine Growth Factors.

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Authors: Kazuhiro Kawamura, Yuan Chen, Yimin Shu, Yuan Cheng, Jie Qiao, Barry Behr, Renee A Reijo Pera, Aaron J W Hsueh

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Public Summary:

This study provides information that may be useful to improvements of in vitro fertilization. The manuscript reports the use of growth factors to improve human embryo development in the clinic.

Scientific Abstract:

Studies using animal models demonstrated the importance of autocrine/paracrine factors secreted by preimplantation embryos and reproductive tracts for embryonic development and implantation. Although in vitro fertilization-embryo transfer (IVF-ET) is an established procedure, there is no evidence that present culture conditions are optimal for human early embryonic development. In this study, key polypeptide ligands known to be important for early embryonic development in animal models were tested for their ability to improve human early embryo development and blastocyst outgrowth in vitro. We confirmed the expression of key ligand/receptor pairs in cleavage embryos derived from discarded human tri-pronuclear zygotes and in human endometrium. Combined treatment with key embryonic growth factors (brain-derived neurotrophic factor, colony-stimulating factor, epidermal growth factor, granulocyte macrophage colony-stimulating factor, insulin-like growth factor-1, glial cell-line derived neurotrophic factor, and artemin) in serum-free media promoted >2.5-fold the development of tri-pronuclear zygotes to blastocysts. For normally fertilized embryos, day 3 surplus embryos cultured individually with the key growth factors showed >3-fold increases in the development of 6-8 cell stage embryos to blastocysts and >7-fold increase in the proportion of high quality blastocysts based on Gardner's criteria. Growth factor treatment also led to a 2-fold promotion of blastocyst outgrowth in vitro when day 7 surplus hatching blastocysts were used. When failed-to-be-fertilized oocytes were used to perform somatic cell nuclear transfer (SCNT) using fibroblasts as donor karyoplasts, inclusion of growth factors increased the progression of reconstructed SCNT embryos to >4-cell stage embryos. Growth factor supplementation of serum-free cultures could promote optimal early embryonic development and implantation in IVF-ET and SCNT procedures. This approach is valuable for infertility treatment and future derivation of patient-specific embryonic stem cells.

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